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EXAMINER	
O'FARRELL, THOMAS JOHN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 12/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/798,718	GUO, BAOCHUAN	
	Examiner	Art Unit	
	Thomas J. O'Farrell	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08/26/04,08/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-22, drawn to methods of determining haplotype structures, classified in class 435, subclass 6.

   II. Claim 23, drawn to a kit for determining haplotypes, classified in class 536, subclass 24.3.

2. The inventions are distinct, each from the other because of the following reasons: Inventions of group 2 and group 1 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the primer polynucleotides of group 2 can be used to encode polypeptides or as antisense polynucleotides, which are not required to practice the methods of group 1. The search for each group presents a serious search burden as the searches for each are not coextensive in scope. Art related to the kit of group 2 would not necessarily retrieve art related to the methods of determining haplotypes of group 1. Additionaly, art related to the method of claim 1 of group 1 which involves obtaining an enriched nucleic acid fraction of one allelic variant and genotyping the fraction to identify alleles would not

necessarily retrieve art related to the kit of group 2 as the method claim 1 of group 1 does not require the kit of group 2.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

4. Because these inventions are distinct for the reasons given above and the search required for each group is not coextensive, restriction for examination purposes as indicated is proper.

5. During a telephone conversation with Sarah Eurek on 11/18/05 a provisional election was made with traverse to prosecute the invention of methods of determining haplotypes structures, claims 1-22. Affirmation of this election must be made by applicant in replying to this Office action. Claim 23 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 3, 4, 5, 12, and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 3, the location in the polynucleotide to be analyzed of the recited "target site" is unclear and therefore it is not clear as to what nucleotide sequence the recited "allele-specific hybridization probe" hybridizes to. Claim 17 recites "the method of claim 2 wherein the genotype of the nucleic acid comprising the target site is determined before one allelic variants of the nucleic acid is extracted from the original nucleic acid sample". The phrase "one allelic variants" is not clear with respect to the number of variants extracted from the sample. Also the "target site" is not defined in claims 17, 1, or 2 and therefore it is unclear as to what nucleotides are genotyped within

the "target site". Regarding claim 12, which is dependent on claim 2, claim 2 does not recite the use of an "allele-specific hybridization probe" and therefore the antecedent basis of the "allele-specific hybridization probe" recited in claim 12 is unclear.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

10. Claims 1, 2, 13, 14, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Fanning et al. (herein referred to as Fanning, (1997), Tissue Antigens, vol. 50, pages 23-31, 07/1997).

Regarding claim 1 reciting "...comprising: obtaining an enriched nucleic acid fraction which comprises from 2 to 30 times more of one allelic variant of the nucleic acid than the other allelic variant of the nucleic acid.....", the examiner interprets the enriched nucleic acid fraction to have *outside* of the range of 2 to 30 times more of one allelic variant of the nucleic acid than the other allelic variant of the nucleic acid. Regarding claim 16 reciting "The method of claim 1 wherein the enriched nucleic acid fraction comprises 3 to 6 times more of the enriched allelic variant than the non-enriched allelic variant" the examiner interprets the enriched nucleic acid fraction to have *outside* of the range of 3 to 6 times more of the enriched allelic variant than the non-enriched allelic variant.

Fanning teaches obtaining an enriched nucleic acid fraction of a haplotype of 3 SNPs that is present at a higher level than the corresponding different haplotype of the same SNP sites by allele-specific PCR (claims 1 and 16; see page 23, column 2, para 2, lines 1-4, Table 2, Figures 1 and 2 of Fanning). Fanning teaches that genotyping the enriched fraction involves observing particular combinations of bands that correspond to amplified nucleic acids containing two specific alleles of a haplotype produced from forward and reverse primers that hybridize to specific alleles of two SNPs (claims 1 and 16; see page 23, column 2, para 2, lines 1-4, Table 2, Figures 1 and 2 of Fanning). Fanning teaches that the enriched nucleic acid fraction is obtained by preferentially amplifying one allelic variant and extracting it by gel electrophoresis (claim 2; see Figure 2 of Fanning). Fanning teaches that the nucleic acid samples used in this methods are

genomic DNA (claims 13 and 14; see page 24, column 1, all of para 3 and Figure 1 of Fanning).

11. Claims 1-5, 7 and 12-17 are rejected under 35 U.S.C. 102(e) as being anticipated by Landers (herein referred to as Landers, US Patent 6,844,154).

Regarding claim 1 reciting "...comprising: obtaining an enriched nucleic acid fraction which comprises from 2 to 30 times more of one allelic variant of the nucleic acid than the other allelic variant of the nucleic acid.....", the examiner interprets the enriched nucleic acid fraction to have *outside* of the range of 2 to 30 times more of one allelic variant of the nucleic acid than the other allelic variant of the nucleic acid. Regarding claim 16 reciting "The method of claim 1 wherein the enriched nucleic acid fraction comprises 3 to 6 times more of the enriched allelic variant than the non-enriched allelic variant" the examiner interprets the enriched nucleic acid fraction to have *outside* of the range of 3 to 6 times more of the enriched allelic variant than the non-enriched allelic variant.

Landers teaches obtaining an enriched nucleic acid fraction that contains more of one allelic variant of a haplotype of two SNPs by hybridization to a probe on a solid support that is specific for one particular allele of one SNP of a haplotype (claims 1-3, 12, and 16; see Figure 3, and column 26, lines 34-45 of Landers). Landers teaches that this complex is hybridized with a probe that specifically binds to a particular allele of the other SNP of the haplotype and genotyping involves detecting a signal from this probe which indicates the presence of particular alleles in both SNPs of the haplotype (claims

1-3, 12, and 16; see Figures 3 and 5 and column 26, lines 60-67 and column 27, lines 1-8 of Landers). Landers teaches that the presence of a second allelic-variant haplotype, which would be at a lower level in the enriched fraction of the first haplotype, can be detected by analogous hybridization with a probe on a solid support that specifically binds to a different allele of the first SNP of the haplotype and detection with a probe that specifically binds to an allele of the second SNP of the haplotype (claims 1-3, 12, and 16; see Figures 3 and 5 and column 26, lines 60-67 and column 27, lines 1-8 of Landers). Landers teaches that cold competitor oligos that hybridize to the other allele of the SNP site that is being detected can be added with the labeled allele-specific probes (claim 15; column 27, lines 10-24 of Landers). Landers teaches that the allele-specific probe used to obtain the enriched nucleic acid fraction can be attached to a first binding partner such as streptavidin which can bind to biotin on the surface of the solid support (claims 3-5; see column 9, lines 11-17 of landers). Landers teaches that the DNA haplotyped by this method can be genomic DNA (claims 13 and 14; see column 8, lines 3-8 of Landers). Landers teaches that the haplotype of the nucleic acids analyzed by this procedure can also be determined by direct sequencing (claim 17; see column 30, lines 31-33 of Landers). Landers teaches that a nucleic acid having a particular allele in the first SNP of the haplotype can be identified by a probe labeled with a particular fluorescent marker and separated from a nucleic acid having another allele of the first SNP by flow cytometry based on the presence of a particular fluorescent marker (see column 16, lines 30-38 of Landers). Landers teaches that once the two nucleic acids having different alleles of the first SNP of the haplotype are separated, each can

be analyzed for the allele at the second SNP (claim 7; see column 16, lines 42-44 of Landers).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1, 2, 6, 13, 14, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fanning.

Regarding claim 1 reciting "...comprising: obtaining an enriched nucleic acid fraction which comprises from 2 to 30 times more of one allelic variant of the nucleic acid than the other allelic variant of the nucleic acid.....", the examiner interprets the enriched nucleic acid fraction to have *within* of the range of 2 to 30 times more of one allelic variant of the nucleic acid than the other allelic variant of the nucleic acid. Regarding claim 6 reciting "....the level of the enriched allelic variant in the enriched nucleic acid fraction is from 1.5 to 100 times greater than the level of the non-enriched allelic variant in the enriched nucleic acid fraction", the examiner interprets the level of the enriched allelic variant in the enriched nucleic acid fraction to be *within* the range of 1.5 to 100 times greater than the level of the non-enriched allelic variant. Regarding

claim 16 reciting "The method of claim 1 wherein the enriched nucleic acid fraction comprises 3 to 6 times more of the enriched allelic variant than the non-enriched allelic variant" the examiner interprets the enriched nucleic acid fraction to have *within* the range of 3 to 6 times more of the enriched allelic variant than the non-enriched allelic variant.

Fanning teaches obtaining an enriched nucleic acid fraction of a haplotype of 3 SNPs that is present at a higher level than the corresponding different haplotype of the same SNP sites by allele-specific PCR (claims 1 and 16; see page 23, column 2, para 2, lines 1-4, Table 2, Figures 1 and 2 of Fanning). Fanning teaches that genotyping the enriched fraction involves observing particular combinations of bands that correspond to amplified nucleic acids containing two specific alleles of a haplotype produced from forward and reverse primers that hybridize to specific alleles of two SNPs (claims 1 and 16; see page 23, column 2, para 2, lines 1-4, Table 2, Figures 1 and 2 of Fanning). Fanning teaches that the enriched nucleic acid fraction is obtained by preferentially amplifying one allelic variant and extracting it by gel electrophoresis (claim 2; see Figure 2 of Fanning). Fanning teaches that the nucleic acid samples used in this methods are genomic DNA (claims 13 and 14; see page 24, column 1, all of para 3 and Figure 1 of Fanning).

Fanning does not teach a method of haplotype analysis wherein the enriched nucleic acid fraction has *specifically 2 to 30 times* more of one allelic variant of the nucleic acid than the other allelic variant of the nucleic acid (claim 1), or wherein the level of the enriched allelic variant in the enriched fraction is *specifically 1.5 to 100 times*

greater than the level of the non-enriched variant (claim 6), or wherein the enriched nucleic acid fraction has *specifically 3 to 6 times* more of the enriched allelic variant than the non-enriched allelic variant (claim 16). However, per MPEP 2144.05, where the general conditions of the claim are disclosed in the prior art, it is not inventive to discover optimum or workable ranges by routine experimentation and it is the normal desire of scientists and artisans to improve on what is already generally known. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made improve the method of haplotype analysis taught by Fanning through routine experimentation to provide optimal or workable ranges, such as where the enriched allelic variant is *specifically 1.5 to 100 times* greater than the level of the non-enriched variant or where the enriched nucleic acid fraction has *specifically 2 to 30 times* more of one allelic variant of the nucleic acid than the other allelic variant of the nucleic acid or where the enriched nucleic acid fraction has *specifically 3 to 6 times* more of the enriched allelic variant than the non-enriched allelic variant, in view of Fanning. The ordinary artisan would have been motivated to improve the method of haplotype analysis taught by Fanning through routine experimentation to provide optimal or workable ranges, such as where the enriched allelic variant is *specifically 1.5 to 100 times* greater than the level of the non-enriched variant or where the enriched nucleic acid fraction has *specifically 2 to 30 times* more of one allelic variant of the nucleic acid than the other allelic variant of the nucleic acid or where the enriched nucleic acid fraction has *specifically 3 to 6 times* more of the enriched allelic variant than

the non-enriched allelic variant, for the purpose of obtaining the optimal range to practice the method of haplotyping taught by Fanning.

14. Claims 1-7 and 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Landers.

Regarding claim 1 reciting "...comprising: obtaining an enriched nucleic acid fraction which comprises from 2 to 30 times more of one allelic variant of the nucleic acid than the other allelic variant of the nucleic acid.....", the examiner interprets the enriched nucleic acid fraction to have *within* of the range of 2 to 30 times more of one allelic variant of the nucleic acid than the other allelic variant of the nucleic acid. Regarding claim 6 reciting "....the level of the enriched allelic variant in the enriched nucleic acid fraction is from 1.5 to 100 times greater than the level of the non-enriched allelic variant in the enriched nucleic acid fraction", the examiner interprets the level of the enriched allelic variant in the enriched nucleic acid fraction to be *within* the range of 1.5 to 100 times greater than the level of the non-enriched allelic variant. Regarding claim 16 reciting "The method of claim 1 wherein the enriched nucleic acid fraction comprises 3 to 6 times more of the enriched allelic variant than the non-enriched allelic variant" the examiner interprets the enriched nucleic acid fraction to have *within* the range of 3 to 6 times more of the enriched allelic variant than the non-enriched allelic variant.

Landers teaches obtaining an enriched nucleic acid fraction that contains more of one allelic variant of a haplotype of two SNPs by hybridization to a probe on a solid

support that is specific for one particular allele of one SNP of a haplotype (claims 1-3, 12, and 16; see Figure 3, and column 26, lines 34-45 of Landers). Landers teaches that this complex is hybridized with a probe that specficially binds to a particular allele of the other SNP of the haplotype and genotyping involves detecting a signal from this probe which indicates the presence of particular alleles in both SNPs of the haplotype (claims 1-3, 12, and 16; see Figures 3 and 5 and column 26, lines 60-67 and column 27, lines 1-8 of Landers). Landers teaches that the presence of a second allelic-variant haplotype, which would be at a lower level in the enriched fraction of the first haplotype, can be detected by analogous hybridization with a probe on a solid support that specifically binds to a different allele of the first SNP of the haplotype and detection with a probe that specifically binds to an allele of the second SNP of the haplotype (claims 1-3, 12, and 16; see Figures 3 and 5 and column 26, lines 60-67 and column 27, lines 1-8 of Landers). Landers teaches that cold competitor oligos that hybridize to the other allele of the SNP site that is being detected can be added with the labeled allele-specific probes (claim 15; column 27, lines 10-24 of Landers). Landers teaches that the allele-specific probe used to obtain the enriched nucleic acid fraction can be attached to a first binding partner such as streptavidin which can bind to biotin on the surface of the solid support (claims 3-5; see column 9, lines 11-17 of Landers). Landers teaches that the DNA haplotyped by this method can be genomic DNA (claims 13 and 14; see column 8, lines 3-8 of Landers). Landers teaches that the haplotype of the nucleic acids analyzed by this procedure can also be determined by direct sequencing (claim 17; see column 30, lines 31-33 of Landers). Landers teaches that a nucleic acid having a particular

allele in the first SNP of the haplotype can be identified by a probe labeled with a particular fluorescent marker and separated from a nucleic acid having another allele of the first SNP by flow cytometry based on the presence of a particular fluorescent marker (see column 16, lines 30-38 of Landers). Landers teaches that once the two nucleic acids having different alleles of the first SNP of the haplotype are separated, each can be analyzed for the allele at the second SNP (claim 7; see column 16, lines 42-44 of Landers).

Landers does teach methods of haplotype analysis wherein the enriched nucleic acid fraction has *specifically 2 to 30 times* more of one allelic variant of the nucleic acid than the other allelic variant of the nucleic acid (claim 1), or wherein the level of the enriched allelic variant in the enriched fraction is *specifically 1.5 to 100 times* greater than the level of the non-enriched variant (claim 6), or wherein the enriched nucleic acid fraction has *specifically 3 to 6 times* more of the enriched allelic variant than the non-enriched allelic variant (claim 16). However, per MPEP 2144.05, where the general conditions of the claim are disclosed in the prior art, it is not inventive to discover optimum or workable ranges by routine experimentation and it is the normal desire of scientists and artisans to improve on what is already generally known. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made improve the method of haplotype analysis taught by Landers through routine experimentation to provide optimal or workable ranges, such as where the enriched nucleic acid fraction has *specifically 2 to 30 times* more of one allelic variant of the nucleic acid than the other allelic variant of the nucleic acid or where the

enriched allelic variant is *specifically 1.5 to 100 times* greater than the level of the non-enriched variant or wherein the enriched nucleic acid fraction has *specifically 3 to 6 times* more of the enriched allelic variant than the non-enriched allelic variant, in view of Landers. The ordinary artisan would have been motivated to improve the method of haplotype analysis taught by Landers through routine experimentation to provide optimal or workable ranges, such as where the enriched nucleic acid fraction has *specifically 2 to 30 times* more of one allelic variant of the nucleic acid than the other allelic variant of the nucleic acid or where the enriched allelic variant is *specifically 1.5 to 100 times* greater than the level of the non-enriched variant or where the enriched nucleic acid fraction has *specifically 3 to 6 times* more of the enriched allelic variant than the non-enriched allelic variant, for the purpose of obtaining the optimal range to practice the method of haplotyping taught by Landers.

15. Claims 8-11 and 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Landers as applied to claims 1-7 and 12-17 above, and further in view of Sorenson (herein referred to as Sorenson, US Patent 6,020,124, 02/2000).

Regarding claim 18 reciting "...the level of the preferentially extracted allelic variant is from 2 to 30 times greater than the level of the allelic variant that is not preferentially extracted from the sample....", the examiner interprets the level of the extracted allelic variant to be *within* of the range of 2 to 30 times greater than the level of the allelic variant that is not preferentially extracted from the sample. Regarding claim 22 reciting "....the amount of the enriched allelic variant in the enriched nucleic

acid fraction is from 3 to 10 times greater than the amount of the non-enriched allelic variant.....", the examiner interprets the amount of the enriched allelic variant in the enriched nucleic acid fraction to be *within* the range of 3 to 10 times greater than the amount of the non-enriched allelic variant.

The teachings of Landers as applied to claims 1-7 and 12-17 are recited in paragraph 14 above.

Landers does not teach a method of haplotyping which involves *amplifying* the nucleic acids in the enriched nucleic acid fraction prior to identifying the alleles of interest (claims 8-11 and 18-22). However, Sorenson teaches that prior to determining the alleles present in a particular nucleic acid, the nucleic acid sample can be amplified with a common amplification step by PCR to amplify wild-type and mutant forms of the DNA to increase the amount of DNA from which the mutant allele can be detected (see column 2, lines 30-39 of Sorenson). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of haplotype identification taught by Landers to include PCR amplification of the nucleic acids in the enriched nucleic acid fraction prior to identifying the alleles of interest by using an amplification that would amplify all of the allelic variants in the same proportion in view of the teachings of Sorrenson. The ordinary artisan would have been motivated to improve the method of haplotype identification taught by Landers to include PCR amplification of the nucleic acids in the enriched nucleic acid fraction prior to identifying the alleles of interest by using an amplification that would amplify all of the allelic variants in the same proportion because Sorenson teaches that a common

amplification step prior to specific allele identification increases the amount of DNA from which mutant alleles can be detected.

Landers in view of Sorenson do not teach methods of haplotype analysis wherein the level of the preferentially extracted allelic variant is *specifically from 2 to 30 times* greater than the level of the allelic variant that is not preferentially extracted (claim 18), or wherein the amount of the enriched allelic variant in the enriched fraction is *specifically 3 to 10 times* greater than the amount of the non-enriched variant (claim 22). However, per MPEP 2144.05, where the general conditions of the claim are disclosed in the prior art, it is not inventive to discover optimum or workable ranges by routine experimentation and it is the normal desire of scientists and artisans to improve on what is already generally known. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made improve the method of haplotype analysis taught by Landers in view of Sorrenson through routine experimentation to provide optimal or workable ranges, such as where the level of the preferentially extracted allelic variant is *specifically from 2 to 30 times* greater than the level of the allelic variant that is not preferentially extracted or where the amount of the enriched allelic variant in the enriched fraction is *specifically 3 to 10 times* greater than the amount of the non-enriched variant in view of Landers. The ordinary artisan would have been motivated to improve the method of haplotype analysis taught by Landers in view of Sorrenson through routine experimentation to provide optimal or workable ranges, such as where the level of the preferentially extracted allelic variant is *specifically from 2 to 30 times* greater than the level of the allelic variant that is not

preferentially extracted or where the amount of the enriched allelic variant in the enriched fraction is *specifically 3 to 10 times* greater than the amount of the non-enriched variant, for the purpose of obtaining the optimal range to practice the method of haplotyping taught by Landers in view of Sorrenson.

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas O'Farrell whose telephone number is (571) 272-8782. The examiner can normally be reached Monday-Friday from 8:30 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Thomas O'Farrell
Examiner
Art Unit 1634

12/09/05

JEHANNE SITTON
PRIMARY EXAMINER

12/9/05